

REMARKS

The following is in response to the Office Action mailed on May 12, 2004 in connection with the above-identified application.

Rejection of Claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 under 35 U.S.C. §103(a)

Claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 have been rejected under 35 U.S.C. §103 as being unpatentable over Fliri *et al.*, (WO 99/09025) and Glass *et al.* (IDS) in view of Fliri *et al.* (US 5,883,094) and Faraci *et al.*, (US 5,889,010). Applicants respectfully disagree.

Applicants submit that to satisfy the legal standard under 35 U.S.C. § 103, an Examiner must identify both (i) a suggestion to modify a primary reference in accordance with the teachings of one or more secondary references to achieve the claimed invention and (ii) a reasonable expectation of success in making and using the modified procedure (*In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991)). Furthermore, both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure (*In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988)). The modification must be more than just "obvious to try", which the Court of Appeals for the Federal Circuit has rejected as a standard for obviousness (*In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988)). Moreover, in combining references, the Examiner may not use an applicant's disclosure as a guide or template to select elements or features from among prior art references which, when assembled together, arrive at the claimed invention (*In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992)).

The Examiner specifically argues (Office Action, point 5, page 2), that Fliri *et al.* (WO 99/09025) teaches that indols, in particular CP-266,269 are D4 agonists; and that Glass *et al.*, (applicants assume that Examiner is referring to the reference of Glase *et al.*, included in Applicants IDS) teaches that benzamides, in particular N-[[4-(2-cyanophenyl)-1-piperazinyl]methyl]-3-methyl benzamide are known D4 agonists. As stated by the Examiner none of the above references teach the use of dopamine D4 to treat sexual dysfunction. Fliri *et al.* (WO 99/09025) teaches compounds useful in a method of treating a series of other disorders involving the dopaminergic system, but not

sexual dysfunction, and Glase *et al.*, teaches the use of D4 agonists as tools useful in understanding the contribution of D4 receptors to schizophrenia.

The Examiner argues that Fliri *et al.*, (US 5,883,094) and Faraci *et al.* (US 5,889,010) teach “compounds having D4 dopaminergic activity are known to be useful for treating sexual dysfunction” (Office Action, point 7, page 3). Both of the cited references teach the usefulness of compounds that are ligands to the dopaminergic D4 receptor. One skilled in the art knows that the terms “dopamine ligands” define compounds only for their capacity to bind to dopamine receptors. The term does not describe the biological activity of the compounds, i.e. if the compounds stimulate, inhibit or have no effect at all after binding to the receptor. Additionally, Faraci *et al.*, teaches that:

“They [The novel compounds of the formula I] are therefore able to function as therapeutic agents in the treatment of a variety of conditions in mammals, the treating or prevention of which can be effected or facilitated by an **increase or decrease** in dopamine mediated neurotransmission” (emphasis added). (Col. 20, lines 40-44).

Accordingly, Faraci *et al.*, does not teach if these compounds of formula (I) are useful at all as agonists, even less as agonists useful to treat sexual dysfunction. Applicants would also like to point out that Claim 5 and Claim6 refer to method and pharmaceutical composition to treat several disorders (including sexual disorders) comprising administering “a dopaminergic effective amount of a compound according to claim I”. Faraci *et al.*, defines “a dopaminergic effective amount” as a compound that inhibit the binding of dopamine to a dopamine receptor (col 9, lines 55-59). This is tantamount to define these compounds as antagonists. The rest of the method claims of Faraci *et al.*, (claims 7-10) refer to the use of compounds in general without any definition of these acting as agonists or antagonists.

Fliri *et al.* (US 5,883,094), uses the same definition for “dopaminergic effective amount” (as used in the claims) as Faraci *et al.* does and as described in the paragraph above. As with Faraci *et al.*, Fliri *et al.*, teaches compounds that can either stimulate or decrease dopaminergic activity without teaching or suggesting that agonists in particular may be useful to treat sexual dysfunction.

Applicants submit that: (A) nowhere in *Fliri et al.* (WO 99/09025) or *Glase et al.*, there is a suggestion that D4 agonists may be used to treat sexual dysfunction; and (B) that *Fliri et al.* (US 5,883,094), fails to teach or suggest that the modification of any of the disclosed compounds may result in the making of a compound useful in treating sexual dysfunction with a reasonable expectation of success.

The dopamine D4 receptor agonists of the present invention induced a stimulation of the sexual behavior in rats, with a reduced emetic effect in the same (emphasis added). The emetic effect has been an unwanted secondary effect present with all previous agonists used to treat sexual dysfunction, as for example with apomorphine. The unexpected lack of emetic effect obtained with the D4 dopaminergic agonists of the present invention is due to the specific action of the compounds of the present invention on the dopamine D4 receptor subtype, rather than on the D2 receptor subtype. This unexpected result is well documented in the specification on pages 13 through 17, and provides further evidence to support the non-obviousness of the present invention over the prior art.

Nowhere in *Fliri et al.*, (WO 99/09025), *Glase et al* (IDS), *Fliri et al.* (US 5,883,094) and *Faraci et al.*, (US 5,889,010) there is a motivation or a suggestion, alone or in combination, to use any of the disclosed compounds to treat specifically sexual dysfunction and obtaining the unexpected results presented in the present invention. It appears that the Examiner merely combines the references without the proper motivation or expectation of success in order to make the obviousness rejection. Applicants respectfully submit that the Office Action appears to be using impermissible hindsight in presenting the obviousness rejection.

As stated in *N.V. Akzo v. E.I. du Pont de Nemours & Co.*, 810 F.2d 1148, 1 USPQ 2d 1704 (Fed. Cir. 1987), “[T]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant’s disclosure”. Thereupon, in view of these arguments, Applicants respectfully request that the rejection of claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 under 35 U.S.C. §103 (a) be withdrawn.

Applicants submit that both rejections of claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 under 35 U.S.C. §103 (a) have been adequately addressed in view of the remarks set above. The Examiner is thus respectfully requested to withdraw the rejection.

Should the Examiner have any concerns regarding the above, he or she is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,
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